UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,669	04/30/2001	Philippe Marliere	205907USOPCT	9510

22850 7590 07/28/2006

C. IRVIN MCCLELLAND
OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 07/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,669	MARLIERE ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *86-104 and 106-118* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *86-102* is/are allowed.

6)☒ Claim(s) *103,104 and 107* is/are rejected.

7)☒ Claim(s) *106 and 108-118* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the amendment, filed 5/1/2006, in which claims 1-85 and 105 were canceled, and claims 86, 103, 104, 106, 108 and 116 were amended. Currently, claims 86-104 and 106-118 are pending and under consideration. Applicant's arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and objections not reiterated in this action have been withdrawn. **This action is FINAL.**

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

Claim 106 is objected to because of the following informalities: the first strain listed in the claim is referred to as strain (b). It would be remedial to amend to the claim to list the strains as strains (a)-(e) rather than strains (b)-(f). Appropriate correction is required. **This is a new objection, necessitated by the amendment to the claims in the reply filed 5/1/2006.**

Claim 108 is objected to because of the following informalities: the word order of the phrase "isolating a protein comprising at least of the one unconventional amino acids present within the culture medium of step (b) from the culture supernatant and/or from the cell pellet" should be improved. It would be remedial to amend the phrase to recite "isolating a protein comprising the at least one unconventional amino acid from the culture supernatant and/or from the cell pellet obtained in (b)." Appropriate correction is required. **This is a new objection, necessitated by the amendment to the claims in the reply filed 5/1/2006.**

Claims 109-118 depend from claim 108 and thus are objected to for the same reasons as applied to claim 108.

Response to Arguments - Claim Objections

The previous objection of claim 106 as failing to further limit the subject matter of a previous claim has been withdrawn in view of Applicant's amendment to the claim.

The previous objection of claims 116-118 as failing to further limit the subject matter of a previous claim has been withdrawn in view of Applicant's amendment to the claims.

Claim Rejections - 35 USC § 112

Claims 103, 104 and 107 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **The grounds of this rejection have been changed in response to Applicants' amendment of the claims in the response filed on 5/1/2006.**

The rejected claims are drawn to bacterial or yeast cells obtained by methods of selection wherein a missense mutation is incorporated into a an essential gene (required for growth of the host cell) at a target codon and the cell is grown under selective conditions wherein 1) the culture medium does not contain a nutrient that will compensate for the lack of a functional copy of the essential gene product, and 2) the culture medium contains an amino acid encoded by the target codon (prior to mutation). Further, the cell must comprise an aminoacyl-tRNA synthetase which

recognizes a given amino acid and which is capable of charging onto one of its associated tRNAs an unconventional amino acid or an amino acid other than said given amino acid, wherein the gene encoding the aminoacyl-tRNA synthetase contains at least one mutation compared with the sequence of the corresponding wild-type gene. The rejected claims thus comprise a set of yeast and bacterial cells that encompass a mutation in any aminoacyl-tRNA synthetase gene, which is capable of mischarging a tRNA in the cell and suppressing a missense mutation in an essential gene.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. The specification describes *E. coli* strains deposited at the CNCM under the Nos. I-2025, I-2026, I-2027, I-2339, I-2340, and I-2341, also referred to as strains β5366, β8144, β8146, β5479, β5485, and β5486, respectively (e.g. pages 7-9). Strain I-2025 (β5366) does not meet the structural or functional limitations of the claims in that the strain is incapable of growing without thymine or thymidine due to the absence of a mutation in any gene capable of suppressing the missense mutation in the thyA gene (e.g. Example 1). Strains I-2026 and I-2027 contain the K277Q allele of the ValS gene (e.g. page 24, lines 23-25). Strain I-2339 contains the R223H allele of the ValS gene (e.g. page 8, lines 13-24). Strain I-2340 contains the V276A allele of the ValS gene (e.g. page 8, lines 25-34). Strain I-2341 contains the D230N allele of the ValS gene (e.g. page 9, lines 7-8). Thus, each of the strains described in the instant specification is a strain of *E. coli* with a missense mutation in the ValS gene. The specification

does not describe mutations in any other *E. coli* aminoacyl-tRNA synthetase genes. The specification does not describe any mutations in an aminoacyl-tRNA synthetase gene of a cell isolated from any other type of organism, either yeast or bacteria. Further, the instant specification and prior art do not clearly describe what mutations in what functional domains of different aminoacyl-tRNA proteins will allow the mutated aminoacyl-tRNA synthetase to function in the manner recited in the rejected claims.

Even if one accepts that the examples described in the specification meet the claim limitations of the rejected claims with regard to structure and function, the examples are only representative of *E. coli* strains with missense mutations in the ValS gene. The results are not necessarily predictive of other mutations that will confer the claimed function. Thus, it is impossible for one to extrapolate from the few examples described herein those isolated cells that would necessarily meet the structural/functional characteristics of the rejected claims.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the genetic modifications required to confer the claimed function, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound

itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Given the very large genus of yeast and bacterial cells encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to genetic modifications of aminoacyl-tRNA synthetase that meet the functional limitations of the claims, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the broadly claimed genus of isolated cells. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention for claims 103, 104 and 107.

Response to Arguments/112 1st Rejection

The rejection of claims 86-118 under 35 U.S.C. 112, first paragraph (enablement), has been withdrawn in view of Applicant's amendment to the claims. The previous rejection of claims 86-118 has been withdrawn.

With respect to the rejection of claims 103, 104 and 107 (written description), Applicant's arguments filed 5/1/2006 have been fully considered but they are not persuasive.

The response notes that the scope of the rejected claims has been narrowed to encompass only yeast and bacterial cells. Further, the response asserts that it would not be an undue burden for one skilled in the art to adapt the teaching provided in the specification concerning valyl-tRNA synthetase (ValS) to other aminoacyl-tRNA synthetase genes. This is not found persuasive because the skilled artisan cannot envision the genetic modifications capable of conferring the claimed function, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). The teachings of the instant specification do not allow one to envision the genetic modifications within other aminoacyl-tRNA synthetase genes that would confer the claimed function.

The response provides evidence in the form of a review article, published prior to the effective filing date of the instant application, that the active sites (editing domain) of aminoacyl-tRNA synthetases are conserved even though the overall topologies of the proteins differ. While the review article by Delarue provides evidence that aminoacyl-tRNA synthetases share a

conserved active site, more than the active site is required to alter the substrate specificity of an aminoacyl-tRNA synthetase. Delarue points out that "Redesigning the amino acid specificity of TyrRS is, however, not a trivial matter" (page 50, paragraph bridging columns). The aminoacyl-tRNA synthetases posses additional domains that help to make them more specific in the tRNA recognitions process (Delarue, page 52), and the mutations in these domains necessary for the claimed function are not described in the instant specification. Thus, one could not envision the genetic changes in any yeast or bacterial aminoacyl-tRNA synthetase gene sufficient to recognize an unconventional amino acid and charge the amino acid onto one of its associated tRNAs.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Conclusion

Claims 86-102 are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached at 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR, http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

jad

CELINE QIAN, PH.D.
PRIMARY EXAMINER